BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.247

Section:	Prescription Drugs	**Effective Date:**	July 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	September 5, 2025
Subject:	Hernexeos	**Page:**	1 of 4

Last Review Date: June 11, 2026

Hernexeos

Description

Hernexeos (zongertinib)

Background
Hernexeos (zongertinib) is a kinase inhibitor of human epidermal growth factor receptor 2 (HER2). In vitro, Hernexeos inhibited phosphorylation of HER2, downstream signaling of HER2 (phosphorylation of ERK), and proliferation of lung cancer cells harboring HER2 tyrosine kinase domain activating mutations. In vivo, Hernexeos demonstrated anti-tumor activity in mouse xenograft models of non-small cell lung cancer harboring HER2 tyrosine kinase domain activating mutations (1).

Regulatory Status
FDA-approved indications: Hernexeos is a kinase inhibitor indicated for the treatment of adult patients with unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations, as detected by an FDA-authorized test (1).

Hernexeos carries warnings regarding hepatotoxicity, left ventricular dysfunction, and interstitial lung disease (ILD)/pneumonitis. Monitor liver function tests including ALT, AST, and total bilirubin at baseline prior to administration, every 2 weeks during the first 12 weeks, then monthly thereafter as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Left ventricular ejection fraction (LVEF) should be evaluated prior to initiating Hernexeos and monitored at regular intervals during treatment as clinically indicated. New or worsening symptoms indicative of ILD/pneumonitis should be monitored. Interrupt, reduce the dose, or permanently discontinue Hernexeos based on severity (1).

Hernexeos can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Hernexeos and for 2 weeks after the last dose (1).

The safety and effectiveness of Hernexeos in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Hernexeos may be considered **medically necessary** if the conditions indicated below are met.

Hernexeos may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC)
    a. Tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations, as detected by an FDA-authorized test

AND ALL of the following:

1. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)/pneumonitis
2. Prescriber agrees to monitor liver function tests including ALT, AST, and total bilirubin prior to initiation, every 2 weeks during the first 12 weeks, and then monthly thereafter as clinically indicated

3. Prescriber agrees to assess left ventricular ejection fraction (LVEF) prior to initiation and at regular intervals during treatment as clinically indicated
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hernexeos and for 2 weeks after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)/pneumonitis
3. Prescriber agrees to monitor liver function tests including ALT, AST, and total bilirubin monthly as clinically indicated
4. Prescriber agrees to assess left ventricular ejection fraction (LVEF) at regular intervals as clinically indicated
5. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hernexeos and for 2 weeks after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 180 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Hernexeos (zongertinib) is a kinase inhibitor indicated in patients for the treatment of unresectable or metastatic non-squamous NSCLC whose tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations. Hernexeos carries warnings regarding hepatotoxicity, left ventricular dysfunction, ILD/pneumonitis, and embryo-fetal toxicity. The safety and effectiveness of Hernexeos in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Hernexeos while maintaining optimal therapeutic outcomes.

References

1. Hernexeos [package Insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2026.
2. NCCN Drugs & Biologics Compendium® Zongertinib 2026. National Comprehensive Cancer Network, Inc. Accessed on April 14, 2026.

Policy History

Date	Action
September 2025	Addition to PA
December 2025	Annual review and reference update
March 2026	Annual review and reference update
April 2026	Per PI update, changed FDA-approved to FDA-authorized and removed requirement for prior systemic therapy
June 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.